REMARKS

In an Office Action dated August 10, 2007, claims 1-8, 11, 13-19, 22-36, 38-40, 53-61 and 133-136, all of the claims then under consideration in the above-referenced U.S. patent application, were rejected, and claim 39 was objected to. In view of the above amendments, the following remarks, and the accompanying documents, Applicants respectfully request reconsideration of this application, and allowance of the claims, as amended.

Claim 39 was objected to because of an informality which has been corrected by amendment above.

Claims 1-8, 11, 23-36, 38-40 and 133-136 were rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. This rejection is respectfully traversed.

In the Office Action, it is stated that the claims are drawn to methods comprising administering a polypeptide or a conservative variant having wound-healing activity, and that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the entire scope of the claimed invention. This is respectfully traversed.

Applicants' description of the invention is quite detailed. Claims 1 and 23 are the only independent claims of the group rejected as failing to comply with the written description requirement. These claims specify a polypeptide comprising amino acid sequence LKKTET or a conservative variant thereof.

The present specification states that polypeptides having actin sequestering or binding capacity, or that can mobilize actin or modulate actin polymerization, as demonstrated by assay or identified by a sequence such as LKKTET, are useful in the present invention. In addition to thymosin β4 (Tβ4), such polypeptides have been identified in the specification from page 9, line 21 through page 10, line 28.

The term "conservative variant" is defined in the specification as denoting "the replacement of an amino acid residue by another, biologically similar residue". Examples of conservative variations include the replacement of a hydrophobic residue such as isoleucine, valine, leucine or methionine for another, the replacement of a polar residue for another, such

as the substitution of arginine for lysine, glutamic for aspartic acids, or glutamine for asparagine, and the like.

Furthermore, LKKTET and conservative variants thereof, as defined above, include an actin-binding region, active variations of which are found in other actin-binding proteins including those set forth in the last paragraph on page 10 of the specification, e.g., gelsolin (FKHVVP), vitamin D binding protein (DBP) (LKERLQ), cofilin (LKSKMI), depactin (LKMKYS), villin (LKKEKG), and beta-actinin (LKHIES).

As further evidence that the inventors had possession of the claimed invention at the time of filing, Applicants are submitting herewith references demonstrating that persons skilled in the art would recognize that other actin-binding or actin-sequestering polypeptides besides thymosin β4 (TB4) can achieve the object of the present invention. The present specification identifies LKKTET as a sequence which is being able to bind to or sequester actin. The specification further points out that actin-binding or actin-sequestering peptides such as peptides containing amino acid sequence LKKTET or conservative variants thereof have activity corresponding to TB4. There is no evidence of record that sheds any doubt on Applicant's disclosure. To the contrary, submitted herewith are a number of references demonstrating corresponding activity of polypeptides containing LKKTET or conservative variants thereof. For example, Rho et al. (2005) identifies the LKKTET sequence as being active in actin binding and sequestration, and as having an important role in maintaining cellular functions, such as cell morphology, proliferation and locomotion (see, e.g., paragraph bridging columns 1 and 2 of the attached Rho et al. publication).

Other references submitted herewith that show the corresponding activity of LKKTET peptides, conservative variants thereof, and other actin-binding or actin-sequestering peptides, include Wyczólkowska et al. (2007), Irobi et al. (2004), Vaduva et al. (1997), Paunola et al. (2002), Hertzog et al. (2004), Vermeulen et al. (2004), Herrmann et al. (2005), Van Troys et al. (1996), Vancompernolle et al. (1991), Eadie et al. (2002) Hannappel (2007), Huff et al. (2001) and Philp et al. (2003).

The enclosed references provide clear evidence from the relevant art that Applicants had possession of the entire scope of the invention at the time of filing.

In view of the above and the enclosed, it is clear that the specification contains a written description in such full, clear, concise and exact terms as to enable any person skilled

in the art to make and use the invention. In view thereof, withdrawal of the rejection under 35 U.S.C. §112, first paragraph, based on the written description requirement, is respectfully requested.

Claims 1-8, 11, 23-36, 38-40 and 133-136 were rejected under 35 U.S.C. §112, first paragraph, on grounds of lack of enablement. This rejection is respectfully traversed.

It is stated in the Office Action that while the specification is enabling for promoting wound-healing with specific peptides *in vivo* for cornea and skin, the specification does not provide enablement for methods of making and using any peptide variants for any type of wound-healing.

First of all, the rejected claims are not directed to any peptide variants, but to LKKTET peptides or conservative variants thereof. The references discussed above and submitted herewith support the disclosure in the specification of the corresponding activities of polypeptides containing LKKTET and conservatives variants thereof.

In addition, the present specification provides abundant disclosure of treating and preventing injury to numerous tissue types besides skin and corneal tissue. There is no evidence of record that sheds any doubt on Applicants' disclosure. To the contrary, submitted herewith are a number of references demonstrating the efficacy of the claimed polypeptides in treatment and prevention of injury to various distinct tissue types. These references include Hannappel (2007), Huff et al. (2001), Choi et al. (2007), Popoli et al. (2007), Sun et al. (2007), Srivastava et al. (2007), Crockford (2007), Smart et al. (2007), Rossdeutsch et al. (2007), Schneider (2004), Bock-Marquette (2004), Hinkel et al. (2007), Choi et al. (2006), Guarnera et al. (2007), Godschalk (2007), and Blain et al. (2002).

The enclosed references provide clear evidence from the relevant art, demonstrating enablement of the invention as claimed. In view thereof, withdrawal of the rejection under 35 U.S.C. §112, first paragraph, on grounds of lack of enablement, is respectfully requested.

Claims 1-3, 5-7, 11, 13-14, 16-18, 22-29, 33-36, 38-39, 53-55, 57-59, 61 and 133-135 were rejected under 35 U.S.C. §102(e) as being anticipated by Mann U.S. Patent No. 6,030,948. Claims 4, 8, 15, 19, 30-32, 40, 56, 60 and 136 were rejected under 35 U.S.C. §103(a) as being unpatentable over Mann, Siebert et al. U.S. Patent No. 5,591,716, Luedders et al. U.S. Patent No. 4,261,982, and Rahim et al. U.S. Patent No. 4,863,906. These rejections are respectfully traversed.

The application which matured into Mann U.S. Patent No. 6,030,948 was filed **December 19, 1997**. Submitted herewith is a Declaration of the inventors under 37 CFR §1.131, antedating the Mann patent. Attached to the Declaration as composite Exhibit A are copies of notes and notebook pages, the originals of which were prepared prior to December 19, 1997. The experiments set forth in Exhibit A were conceived, supervised and/or conducted by the inventors in the United States. The notes presented in composite Exhibit A show experiments on rats receiving punch wounds, in which Thymosin beta 4 (Tβ4) was administered to the wounded rats topically (directly) or by IP injection, to promote wound healing in the rats. The Exhibit A notes indicate that Tβ4 promoted wound healing in the wounded rats, with increased cell migration, increased cell proliferation, complete epitheliazation and new vascularization. The experiments recorded in the notes of composite Exhibit A were performed in the United States, and establish conception and reduction to practice of the invention set forth in the claims of the present application prior to December 19, 1997, the filing date of the Mann patent.

In view of the Declaration being submitted herewith, the Mann patent has been removed as a prior art reference against the claims of the present application. Accordingly, the rejection based on anticipation by Mann must be withdrawn.

As to the obviousness rejection, the Siebert et al., Luedders et al. and Rahim et al. references cannot be combined to render the present claims unpatentable, since no combination of these references discloses or renders obvious the present claims.

In view of the above Remarks and the accompanying Declaration, withdrawal of the rejections under 35 U.S.C. §102 and 103 is respectfully requested.

The Office Action contains several obviousness-type double patenting rejections. Applicants agree to file appropriate terminal disclaimers, or cancel conflicting claims from other applications, upon an indication that claims of the present application are otherwise allowable.

Also submitted herewith is a Form PTO-1449, listing the references discussed herein and submitted herewith.

It is noted with thanks that claims 13-19, 22 and 53-61 have not be rejected under 35 U.S.C. §112. Since the rejections under 35 U.S.C. §102 and §103 have been overcome, it is respectfully requested that these claims be indicated to contain allowable subject matter.

New claims 173-176 are dependent on previously pending claims, and define the concentrations of the polypeptide in the composition as set forth in the Examples.

Additionally, new independent claims 177-182 are being added, which are believed to define patentable subject matter.

In view of the above amendments and remarks, and the documents submitted herewith, Applicants respectfully request reconsideration of this application.

Respectfully submitted,

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